

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Withdrawn) A transgenic mouse comprising:

- a) a disrupted H2 class I gene;
- b) a disrupted H2 class II gene; and
- c) a functional HLA class I or class II transgene.

2.-7. (Cancelled)

8. (Currently Amended) A method of simultaneously identifying the presence of one or more epitopes in a candidate antigen or group of antigens, wherein the epitope elicits a specific humoral response, a TH HLA-DR1 restricted response, and/or a CTRL HLA-A2 restricted response, the method comprising:

a) administering the candidate antigen or group of candidate antigens to the ~~a transgenic mouse of claim 3 or claim 6 deficient for both H2 class I and class II molecules, wherein the transgenic mouse comprises a functional HLA class I transgene and a functional HLA class II transgene;~~

b) assaying for a specific humoral response in the mouse to the antigen;

c) assaying for a TH HLA-DR1 restricted response in the mouse to the antigen; and

d) assaying for a GTRL HLA-A2 restricted response in the mouse to the antigen; wherein,

observation of a specific humoral response in the mouse to the antigen identifies an epitope which elicits a humoral response in the antigen;

observation of a TH HLA-DR1 restricted response in the mouse to the antigen identifies an epitope which elicits a TH HLA-DR1 restricted response in the antigen; and

observation of a GTRL HLA-A2 restricted response in the mouse to the antigen identifies an epitope which elicits a GTRL HLA-A2 restricted response in the antigen; and

wherein the HLA class I transgene is an HLA-A2 transgene and the HLA class II transgene is an HLA-DR1 transgene, or

the transgenic mouse has the genotype HLA-A2⁺HLA-DR1⁺β2m^oIAβ^o.

9. (Original) The method of claim 8, further comprising assaying for a Th1-specific response in the mouse to the antigen and assaying for a Th2-specific response in the mouse to the antigen; wherein

observation of a Th1-specific response in the mouse to the antigen identifies an epitope which elicits a Th1-specific response in the mouse to the antigen; and

observation of a Th2-specific response in the mouse to the antigen identifies an epitope which elicits a Th2-specific response in the mouse to the antigen.

10. (Currently amended) A method of identifying the presence of an HLA DR1-restricted T helper epitope in a candidate antigen or group of candidate antigens, the method comprising:

a) administering the candidate antigen or group of candidate antigens to the a transgenic mouse of claim 3 or claim 6 deficient for both H2 class I and class II molecules, wherein the transgenic mouse comprises a functional HLA class I transgene and a functional HLA class II transgene; and

b) assaying for a TH HLA-DR1 restricted T helper epitope response in the mouse to the antigen; wherein,

observation of a TH HLA-DR1 restricted T helper epitope response in the mouse to the antigen identifies an epitope which elicits a TH HLA-DR1 restricted T helper epitope response in the antigen; and

wherein the HLA class I transgene is an HLA-A2 transgene and the HLA class II transgene is an HLA-DR1 transgene, or

the transgenic mouse has the genotype HLA-A2⁺HLA-DR1⁺β2m°IAβ°.

11. (Withdrawn) An isolated antigen comprising an HLA DR1-restricted T helper epitope identified by the method of claim 10.

12. (Withdrawn) The isolated antigen of claim 11, wherein the antigen further comprises an epitope which elicits a humoral response and/or an epitope which elicits a CTRL HLA-A2 restricted response.

13. (Withdrawn) The isolated antigen of claim 11, wherein the antigen comprising an HLA DR1-restricted T helper epitope comprises a polypeptide.

14. (Withdrawn) The isolated antigen of claim 11, wherein the antigen comprising an HLA DR1-restricted T helper epitope comprises a polynucleotide.

15. (Withdrawn) The isolated antigen of claim 14, wherein the antigen comprising an HLA DR1-restricted T helper epitope comprises, DNA, RNA, or DNA and RNA.

16. (Original) A method of identifying the presence of an HLA-A2-restricted T cytotoxic (CTL) epitope in a candidate antigen or group of candidate antigens, the method comprising:

a) administering the candidate antigen or group or candidate antigens to the mouse of claim 3 or claim 6; and

b) assaying for an HLA-A2-restricted T cytotoxic (CIL) response in the mouse to the antigen or group of antigens; wherein,

observation of an HLA-A2-restricted T cytotoxic (CTL) response in the mouse to the antigen or group of antigens identifies an epitope which elicits a an HLA-A2 restricted T cytotoxic (eTL) response in the antigen group of antigens.

17. (Withdrawn) An isolated antigen comprising an HLA-A2-restricted T cytotoxic (CTL) epitope identified by the method of claim 16.

18. (Withdrawn) The isolated antigen of claim 17, wherein the antigen further comprises an epitope which elicits a humoral response and/or an epitope which elicits a TH HLA-DR1 restricted T helper epitope response.

19. (Withdrawn) The Isolated antigen of claim 17, wherein the antigen comprising an HLA-A2-restricted cytotoxic (CTL) epitope comprises a polypeptide.

20. (Withdrawn) The isolated antigen of claim 17, wherein the antigen comprising an HLA A2-restricted T cytotoxic (CTL) epitope comprises 'a polynucleotide.

21. (Withdrawn) The isolated antigen of claim 20, wherein the antigen comprising an HLA-A2-restricted T cytotoxic (CTL) epitope comprises, DNA, RNA, or DNA and RNA.

22. (Withdrawn) A method of comparing the efficiency of T-helper cell response induced by two or more vaccines, the method comprising:

- a) administering a first candidate vaccine to a mouse of claim 3 or claim 6 and measuring the T-helper cell response induced in the mouse by the first candidate vaccine;
- b) administering a second candidate vaccine to a mouse of claim 3 or claim 6 and measuring the T-helper cell response induced in the mouse by the second candidate vaccine;
- c) administering each additional candidate vaccine to be compared to a mouse of claim 3 or claim 6 and measuring the T-helper cell response Induced in the mouse by each additional candidate vaccine to be compared; and
- d) determining the efficiency of each candidate vaccine to Induce a T-helper cell response by comparing the T-helper cell responses to each of the vaccines to be compared with each other.

23. (Withdrawn) The method of claim 22, wherein the T-helper cell response Is an HLA DR1 restricted response.

24. (Withdrawn) A method of comparing the efficiency of T cytotoxic cell response induced by two or more vaccines, the method comprising:

- a) administering a first candidate vaccine to a mouse of claim 3 or. .

claim 6 and measuring the T cytotoxic cell response induced In the mouse by the first candidate vaccine;

b) administering a second Candidate vaccine to a mouse of claim 3 or claim 6 and measuring the T cytotoxic cell response induced in the mouse by second candidate vaccine;

c) administering each additional candidate vaccine to be compared to a mouse of claim 3 or claim 6 and measuring the T cytotoxic cell response induced In the mouse by each additional candidate vaccine to be compared; and

d) determining the efficiency of each candidate vaccine to induce a T cytotoxic cell response by comparing the T cytotoxic cell responses to each of the vaccines to be compared with each other.

25. (Withdrawn) The method of claim 24, wherein the T cytotoxic cell response is an HLA-A2 restricted response.

26. (Withdrawn) A method of simultaneously comparing the efficiency of T-helper cell response and T cytotoxic cell response induced by two or more vaccines, the method comprising:

a) administering a first candidate vaccine to a mouse of claim 3 or . claim 6 and measuring the T-helper cell response and T cytotoxic cell response induced in the mouse by the first candidate vaccine;

b) administering a second candidate vaccine to a mouse of claim 3 or claim 6 and measuring the T-helper cell response and T cytotoxic cell response induced in the mouse by the second candidate vaccine;

- c) administering each additional candidate vaccine to be compared to a mouse of claim 3 or claim 6 and measuring the T-helper cell response and T cytotoxic cell response induced in the mouse by each additional candidate vaccine to be compared; and
- d) determining the efficiency of each candidate vaccine to induce a T-helper cell response and T cytotoxic cell response by comparing the T-helper cell response and T cytotoxic cell response to each of the vaccines to be compared with each other.

27. (Withdrawn) The method of claim 26, wherein the T-helper cell response is an HLA-DR1 restricted response, and wherein the T cytotoxic cell response is an HLA-A2 restricted response.

28. (Withdrawn) A method of simultaneously determining the humoral response, the T-helper cell response, and the T cytotoxic cell response of a mouse following its immunization with an antigen or a vaccine comprising one or more antigens, the method comprising:

- a) administering the antigen or the vaccine comprising one or more antigens to a mouse of claim 3 or claim 6;
- b) assaying for a specific humoral response in the mouse to the antigen or vaccine comprising one or more antigens;
- c) assaying for a T-helper cell response in the mouse to the antigen or vaccine comprising one or more antigens; and
- d) assaying for a T cytotoxic cell response in the mouse to the antigen or vaccine comprising one or more antigens.

29. (Withdrawn) The method of claim 28, wherein the T-helper cell response is a TH HLADR1 restricted response.

30. (Withdrawn) The method of claim 28, wherein the T cytotoxic cell response is a CTRL HLA-A2 restricted response.

31. (Withdrawn) A method of optimizing two or more candidate vaccine compositions for administration to a human, based on preselected criteria, the method comprising:

simultaneously determining the humoral response, the T-helper cell response, and the T cytotoxic cell response of a mouse following its immunization with the two or more candidate vaccine compositions, according to claim 28; and

selecting an optimized vaccine by applying preselected criteria to the results.

32. (Withdrawn) The method according to claim 31, wherein the two or more candidate vaccines differ only in the ratio of antigen to adjuvant present in the vaccine.

33. (Withdrawn) The method according to claim 31, wherein the two, or more candidate vaccines differ only in the type of adjuvant present in the vaccine.

34. (Withdrawn) A method of determining whether a vaccine poses a risk of induction of an autoimmune disease when administered to a human, the method comprising:

- a) administering the vaccine to a mouse of claim 3 or claim 6; and
- b) assaying for an autoimmune response in the mouse; wherein

observation of an autoimmune response in the mouse indicates that the vaccine poses a risk of induction of an autoimmune disease when administered to a human.

35. (Withdrawn) An isolated transgenic mouse cell comprising:

- a) a disrupted H2 class I gene;
- b) a disrupted H2 class II gene; and 'c) a functional HLA Class I or class II transgene.

36.-41. (Cancelled)